

Growing Perivascular Epithelioid Cell Tumor of the Liver Studied With Contrast-Enhanced Ultrasonography and Magnetic Resonance Imaging

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Perivascular epithelioid cell tumors (PEComas) are mesenchymal tumors with a usually benign biological behavior.^{1,2} Perivascular epithelioid cell tumors constitute a family of mesenchymal neoplasms that include angiomyolipoma (AML), lymphangiomyomatosis, clear cell “sugar” tumors of the lung, and clear cell myomelanocytic tumors, arising in visceral and soft tissue; all show the presence of a particular cell type, known as a perivascular epithelioid cell. Angiomyolipoma of the liver belongs to this family, usually shows a prevalent component of large epithelioid cells, and is most frequently a slow-growing benign lesion.¹⁻⁴

We report a case of a rapidly growing liver PEComa in a patient with melanoma. Contrast-enhanced ultrasonography (CEUS), magnetic resonance imaging (MRI) with a hepatospecific contrast medium, and histologic examination were performed. During the follow-up, the dimensional increase and history of melanoma led to surgery, and a PEComa with no signs of malignancy was confirmed.

Abbreviations

AML, angiomyolipoma; CEUS, contrast-enhanced ultrasonography; FNH, focal nodular hyperplasia; MRI, magnetic resonance imaging; PEComa, perivascular epithelioid cell tumor

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Case Report

A 46-year-old woman was referred to our institute for an ultrasonographic examination of her abdomen as part of her follow-up after resection of a melanoma from her left leg. Abdominal ultrasonography (Acuson Sequoia; Siemens Medical Solutions, Mountain View, CA) showed a focal hepatic lesion of 35 mm in the third segment, close to the anterior profile, deforming the liver contour.

The lesion was round and mostly hyperechoic with a hypoechoic halo, characterized by peripheral radiating vascularization on color Doppler imaging. Contrast-enhanced ultrasonography was performed by intravenous administration of a sulfur hexafluoride microbubble contrast medium (SonoVue; Bracco SpA, Milan, Italy) in a 2.4-mL bolus followed by a 5-mL saline flush. A 3.5-MHz convex probe was used, with a mechanical index of 0.12.

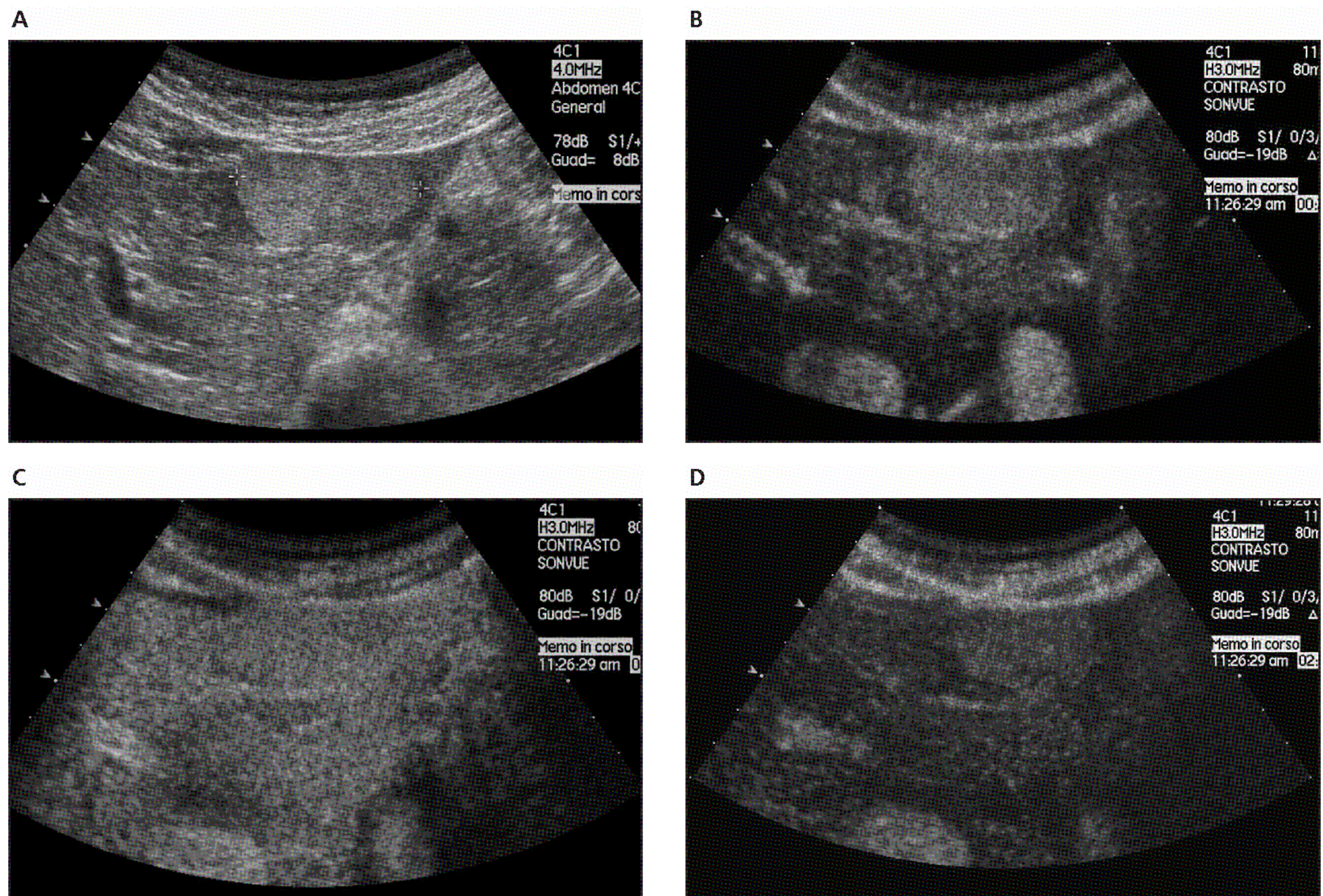
The lesion appeared clearly hypervascular during the arterial phase (6–25 seconds from the beginning of SonoVue injection) and isoechoic in the portal phase (25–90 seconds), and it retained the contrast medium in the equilibrium phase (90–300 seconds) with subsequent hyperechogenicity (Figure 1).

The initial diagnosis was that it might be focal nodular hyperplasia (FNH) because of the hyperechogenicity and the vascular pattern, but because of the history of melanoma, MRI was suggested to better characterize the mass. Abdominal MRI was performed (1-T Signa Horizon LX; GE Healthcare, Milwaukee, WI) with axial T1-weighted spin echo, T2-weighted fast spin echo, and spoiled gradient echo sequences under basal conditions and with dynamic phases after intravenous

administration of a hepatospecific paramagnetic gadobenate dimeglumine contrast medium (MultiHance; Bracco SpA) with and without selective fat tissue signal suppression.

The lesion appeared strongly hyperintense on T2-weighted pulse sequences and hypointense on T1-weighted sequences and showed no notable signal drop on T1-weighted sequences with fat tissue suppression; after injection of the contrast medium, it showed homogeneous and intense contrast enhancement in the arterial phase and persisted as slightly hyperintense in the portal phase. Two hours later in the hepatobiliary excretion phase, the lesion had a marked hypointense appearance to the surrounding parenchyma, indicating the lack of any hepatobiliary function (Figure 2).

Figure 1. **A**, Baseline sonogram showing a well-defined hyperechoic lesion with regular margins and no hypoechoic rim. **B**, Contrast-enhanced sonogram in the arterial phase showing high homogeneous hyperenhancement in comparison with the adjacent liver parenchyma. **C**, Contrast-enhanced sonogram in the portal phase showing complete isoechogenicity. **D**, Contrast-enhanced sonogram in the late phase showing weak protracted hyperechogenicity.



The findings suggested a benign lesion such as FNH or adenoma. Focal nodular hyperplasia was excluded because of the absence of hyperintensity in the hepatobiliary excretion phase. The above-mentioned findings could have been suggestive of hepatic adenoma, but the history of melanoma indicated further investigation to exclude the metastatic nature of the lesion.

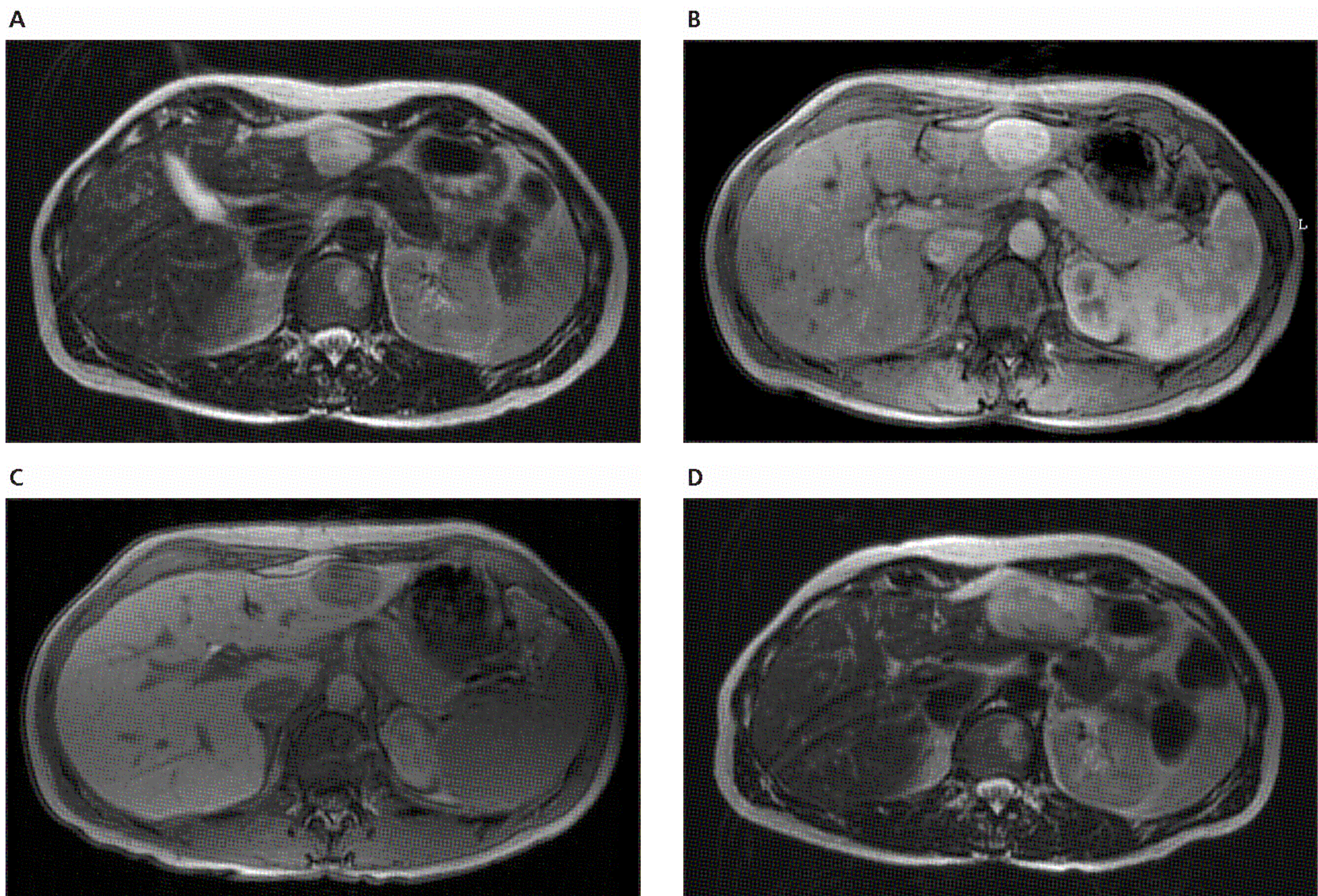
Therefore ultrasonographically guided biopsy was performed with an 18-gauge core biopsy needle (Easy Core; Boston Scientific Corporation, Natick, MA). The neoplastic cells showed immunoreactivity for smooth muscle actin, human melanoma black 45, and melan A and negative findings for S-100 protein and desmin. On the basis of the morphologic characteristics and immunohistochemical results, a diagnosis of PEComa was made.

A wait-and-see attitude was subsequently adopted, with the recommendation of imaging follow-up. Five months later, ultrasonography showed lesion growth of approximately 60% in diameter (from 3.2 to 5.3 cm). This finding was confirmed by further abdominal MRI (Figure 2). Despite the histologic diagnosis of a benign lesion, its rapid growth and the patient's neoplastic history indicated surgical resection. A II-III segmentectomy was performed, and the specimen analysis documented a PEComa with no infiltration of the margins and no cellular signs of malignancy (Figure 3).

Discussion

The term *perivascular epithelioid cell* unifies a class of tumors that share the presence of smooth

Figure 2. Abdominal MRI showing the focal lesion in the left hepatic lobe. **A**, T2-weighted axial sequence showing strong hyperintensity of the lesion. **B**, T1-weighted sequence acquired during the arterial phase after contrast medium injection showing bright homogeneous contrast enhancement. **C**, Marked hypointensity of the surrounding parenchyma 2 hours later. **D**, Axial T2-weighted sequence obtained 5 months later showing the increased size of the lesion.



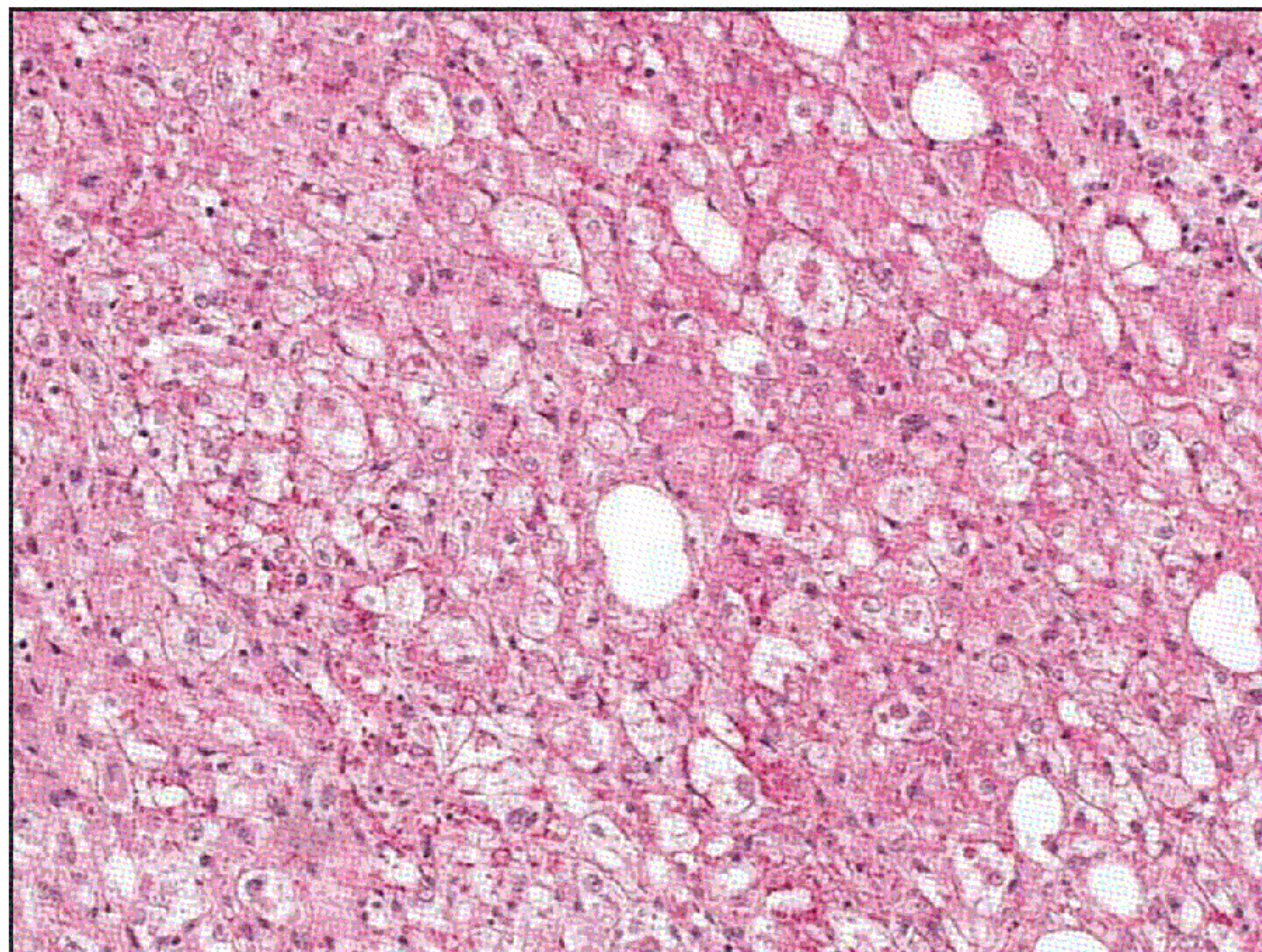


Figure 3. Histopathologic specimen showing pleomorphic epithelioid clear cells intermingled with fat and vascular tissue (hematoxylin-eosin, original magnification $\times 200$).

muscle and melanocytic differentiation. These tumors include AML, lymphangioliomyomatosis, clear cell sugar tumors, and clear cell myomelanocytic tumors.⁵

Perivascular epithelioid cell tumors have been reported in the gastrointestinal tract, falciform ligament, pancreas, bile duct, kidney, pelvic wall, uterus, vulva, prostate, skull, and heart.⁶ A hepatic PEComa is a rare entity, usually considered benign and composed of fat tissue, smooth muscle cells, and proliferative blood vessels, which may have various degrees of soft tissue attenuation depending on the proportion of composition structures, sometimes even including pleomorphic cells.³

The typical ultrasonographic appearance, as described in the literature, is of a round lesion, hyperechoic in up to 90% of cases,⁴ with no posterior acoustic enhancement and high vascularization. As far as we know, the only case of a PEComa studied with CEUS was reported by Flor et al,⁷ in which hepatic AML on dynamic CEUS was described as a highly enhancing lesion with rapid wash-out and which was hypoechoic in the late phase.

In our case, CEUS showed homogeneous hyperechogenicity in the arterial phase without a peripheral ring, isoechogenicity in the portal phase, and slight hyperechogenicity in the equi-

librium phase in comparison with the surrounding hepatic parenchyma, representing the prolonged persistence of the contrast medium in its vascular structures (these features can be found in benign lesions such as FNH and hypervascular adenoma metastases).⁸

The hypervascular pattern was also confirmed by MRI. The diagnosis of FNH was excluded because of the late hypointensity after the injection of the liver-specific contrast material, indicating the lack of uptake by hepatocytes within the mass and the lack of excretion into poorly draining malformed bile ducts considered typical of these benign lesions.^{9,10} The absence of a notable signal drop on fat-saturated pulse sequences was consistent with what has been reported in the literature, where no notable fatty component was detected in 43% of cases.³

The CEUS and MRI features and the patient's sex (female) could suggest a diagnosis of hepatocellular adenoma, although there was no hormonal therapy in the anamnesis. Nevertheless, in a patient with a history of melanoma, the presence of hypervascular metastasis could not be excluded, and ultrasonographically guided biopsy was therefore performed.¹¹

Histologic examination documented no mitoses, evidence of necrosis, or substantial nuclear pleomorphism. Moreover, the immunoreactivity for human melanoma black 45, melan A, and smooth muscle actin is the reference criterion for diagnosis of liver PEComas. Morphologic features are quite similar to those of melanoma, with pleomorphic epithelioid clear cells intermingled with fat tissue and vascular and myoid tissue proliferation¹²; these histological findings, together with the dimensional increase, justified the surgical resection, which confirmed the diagnosis of a PEComa with no evidence of malignancy.

Confident data on dimensional increase curves of benign liver PEComas are lacking in the literature. The growth behavior was described for a PEComa of the kidney in association with tuberous sclerosis.³ In such patients, L'Hostis et al¹² observed the presence of both progesterone and estrogen receptors in the histologic specimens.

The PEComa of the liver in a young woman reported here had impressively rapid growth, with an approximate 60% increase in diameter within 5 months. Liver resection was performed

to achieve a definitive histologic assessment and also with curative intent, in the eventuality that the lesion might be a metastasis.

It is important to determine the unusual biological behavior of this tumor, especially in the context of a history of melanoma, by documenting the possible imaging findings and to consider them within the differential diagnosis; in fact, CEUS showed a different pattern than the only case described in literature, with no rapid wash-out but with persistent slight hyperechogenicity in the equilibrium (late) phase.

The diagnosis of hepatic PEComas may be difficult, especially in monotypic epithelioid forms. Nevertheless, up to now, they often require surgical treatment because reliable criteria of benignity are lacking, especially with imaging modalities.

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